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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/045,732	03/20/1998	CARL W. FULLER	233/127	1331

7590 10/08/2002  
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EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/045,732

Applicant(s)

FULLER ET AL.

Examiner

Marjorie A. Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☒ Claim(s) 10,12,16 and 18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

***Continued Prosecution Application***

The request filed on 5/3/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/045,732 is acceptable and a CPA has been established. An action on the CPA follows.

No amendments or arguments to overcome the objections and rejections of record were filed with the CPA, and none have been received by the examiner as of the date of this Office Action, therefore all of the objections and rejections previously set forth in the office action of 5/3/00 are maintained. A copy of the substance of the office action of 5/3/00 is reiterated below for applicant's convenience.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Specification***

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Revision of the content of the abstract is required on a separate sheet.

***Claim Objections***

Claims 10, 12, 16, 18 are objected to because of the following informalities: Claim 10 describes the compound "deoxyguanosine" and claim 12 describes the compound "deoxyguanisine". Both terms appear to be misspelled. Claim 16 duplicates the word "is" and claim 18 duplicates the word "wherein". Appropriate correction is required.

***Double Patenting***

Applicant is advised that should claims 5 and 6 be found allowable, claims 17 and 18, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

***Claim Rejections - 35 USC § 112***

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. "Propyl-7-deaza-2'-deoxyguanosine" in Claim 11 is not described in the specification which instead describes "7-propyl-7-deaza-2'-deoxyguanosine".

***Claim Rejections - 35 USC § 102***

Claims 1-4, 7-11, 13, 15-16, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilead Sciences, Inc (PCT publication WO 93/09127, 5/13/93, IDS reference AE).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) teaches on page 7 a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the instant invention. The R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III in which the R5 group of analog II described by Gilead Sciences is H, lower alkyl (1-4C), CN, Br, Cl, F, CONR<sub>2</sub>, lower alkenyl (1-4C) or lower alkynyl (1-4C). The R1 group of the molecule of formula II recited in the claimed molecule is a C<sub>1-10</sub> alkyl group optionally substituted by hydroxyl, amino, C<sub>1-4</sub> alkoxy or halo as recited in Claim 1, for example. Likewise, the R3 group of the molecule of formula III is a C<sub>2-10</sub> alkynyl group as recited in Claim 19, for example. Analog II disclosed by Gilead Sciences, Inc. anticipates the molecule of formula II in the present invention as, for example, a C<sub>4</sub> alkyl substituted as R5 in analog II would anticipate such a molecule with a like alkyl substituted for R1 in the molecule of formula II or a C<sub>4</sub> alkynyl substituted as R3 in the molecule of formula III in the present invention. Furthermore, analog II disclosed by Gilead Sciences encompasses the claimed molecules of both claim 10 and 11 in the present invention, R5 being an ethyl group or propyl group, respectively. Also, Gilead Sciences discloses the incorporation of analogs of structural formula II, wherein R5 is hereinbefore described, into oligomers designed for triple-helix formation with a complementary duplex DNA strand thus anticipating claim 16 in which the base of the same structure as that described by Gilead is used in a deoxyribonucleic acid sequence. Further, the oligonucleotides or oligomers of Gilead include DNA or RNA (page 10, lines 14-21).

***Claim Rejections - 35 USC § 103***

Claims 1-4, 7-13, 15-16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93) in view of Li

Art Unit: 1631

(Nucleic Acids Research, 1993, Vol.21, Nol.11, pages 2709-2714) and in further view of Seela and Thomas (Helvetica Chimica Acta, Feb 22, 1995, Vol.78, pages 94-108).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the claimed invention wherein the R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III. The R5 group of analog II described by Gilead Sciences is H, lower alkyl (1-4C), CN, Br, Cl, F, CONR2, lower alkenyl (1-4C) or lower alkynyl (1-4C).

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) does not disclose the molecule wherein the R5 group is a higher alkyl C(5-10).

Li (Nucleic Acids Research, 1993, Vol.21, Nol.11, pages 2709-2714) discloses a method of resolving band compression on electrophoretic bands by substituting a purine base with an analog and destabilization of the oligonucleotide. Li discloses improvement in band compression would be accomplished by substituting with N4-methyl-dCTP and teaches prior studies done using 7-deaza-dGTP analogs. Li also suggested the use of more bulky alkyl groups.

Li does not further disclose additional substitutions on purine or pyrimidine bases.

Seela and Thomas (Helvetica Chimica Acta, Feb 22, 1995, Vol.78, pages 94-108) disclose a method of stabilization of DNA through substitutions on pyrimidine bases with methyl groups. Seela and Thomas state that small pyrimidine 5-substituents have steric freedom in the major groove of B-DNA but that if their size is increased, then structural changes occur to decrease the T<sub>m</sub> and hence their stability. Seela and Thomas further teach a similar situation in 7-substituted 7-deazapurines.

One of ordinary skill in the art would have been motivated to utilize a substituent larger than a methyl group on a 7-substituted 7-deazapurine because the compound previously disclosed by Gilead Sciences uses a C(1-4) substituent while Li taught the substitution of a methyl group in the resolution of compression artifact on electrophoretic gels while suggesting the use of larger groups despite potential problems with false stops. Further, as per teachings of Seela and Thomas, oligonucleotide stability is decreased with substitutions on pyrimidine bases with methyl groups and if the size of the pyrimidine substituents is increased then steric freedom in the major groove of B-DNA is hindered and stability would decrease. Seela and Thomas also stated that this principle is applicable to 7-substituted 7-deazapurines. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, motivated by resolving band compression of electrophoretic bands, to perform the teachings of Li on the analog of Gilead Sciences by substitution of bases and substituting larger groups on 7-substituted 7-deazapurines to increase instability thereby improving resolution of band compression of electrophoretic bands of the oligonucleotide as per the teachings of Seela and Thomas.

Claim 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE), Inc in view of Stryer (Biochemistry, 3<sup>rd</sup> Ed., 1988, W.H. Freeman & Col, New York)

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule for incorporation into oligomers as described above.

Gilead Sciences does not demonstrate the use of the nucleoside/nucleotide molecule in a method for determining the nucleotide base sequence of a DNA molecule.

Stryer discloses methods of DNA sequencing using nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the nucleotide analog of Gilead Sciences in DNA sequencing because DNA sequencing was demonstrated to be successful with nucleotides through the teachings of Stryer. One of ordinary skill in the art would therefore have been motivated to apply known DNA sequencing techniques to the nucleotide analog of Gilead Sciences with a reasonable expectation of success.

Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) in view of Mathews, Christopher; Biochemistry, Benjamin/Cummings Publishing Company, Inc., 1990.

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule and the incorporation of the molecules into oligomers as described above.

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) does not demonstrate the method of elongation of an oligonucleotide sequence (incorporation of molecules into oligomers).

Mathews discloses the method of polynucleotide chain elongation with DNA polymerase and nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the nucleotide of Gilead Sciences in the elongation of an oligonucleotide sequence because Gilead Sciences demonstrates the incorporation of the nucleotide molecules into oligomers and Mathews provides the means in which incorporation of the nucleotide molecules into oligomers would be accomplished successfully. The base analog was known in the art through the teachings of Gilead Sciences who also taught the incorporation of the



Art Unit: 1631

analogues into polynucleotides. Chain elongation procedures were demonstrated to be successful in incorporation of nucleotides into oligomers through the teachings of Mathews. Thus, one of ordinary skill in the art would have been motivated through the combined teachings of Gilead Sciences and Mathews to incorporate the nucleotide analogues of Gilead Sciences into oligomers by utilizing chain elongation procedures of Mathews with a reasonable expectation of success.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) in view of Carey, Francis A., Organic Chemistry, 2nd Edition, McGraw Hill, 1992 .

Gilead Sciences, Inc (PCT publication W0 93/09127, 5/13/93, IDS reference AE) discloses a nucleoside/nucleotide molecule for incorporation into oligomers designed for triple-helix formation with a complementary duplex DNA strand wherein R5, corresponding to R1 in the claimed molecule (II) and R3 in the claimed molecule (III), is a C<sub>1-4</sub> alkyl or C<sub>2-10</sub> alkynyl group, respectively. Gilead Sciences further discloses a synthesis method for said molecule using a "suitably protected nucleotide" (page 22, line 6 and 15).

Gilead Sciences does not disclose the distinct process for the preparation of the molecule (II).

Carey discloses the concepts of protection groups and reduction in the synthesis of organic compounds.

One of ordinary skill in the art would have been motivated to apply organic chemistry principles as set forth by Cary to synthesize molecule II disclosed by Gilead Sciences wherein R5 is a lower alkyl (1-4C) from molecule II disclosed by Gilead Sciences wherein R5 is a lower alkynyl (1-4C) because the molecule was known in the art through the teachings of Gilead Sciences and synthesis steps were also known in the art through the teachings of Carey. It

Art Unit: 1631

would have been obvious to one of ordinary skill in the art at the time the invention was made to rely on the synthesis methods set forth by Carey to synthesize the molecule of Gilead Sciences with a reasonable expectation of success.

### ***Conclusion***

Claims 1-19 are rejected; claims 10, 12, 16, 18 are objected to, and a new abstract is required.

This is a CPA of applicant's earlier Application No. 09/045,732. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

Art Unit: 1631

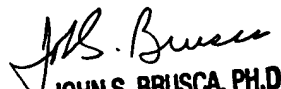
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.



Marjorie A. Moran  
Examiner  
Art Unit 1631

October 4, 2002



JOHN S. BRUSCA, PH.D  
PRIMARY EXAMINER